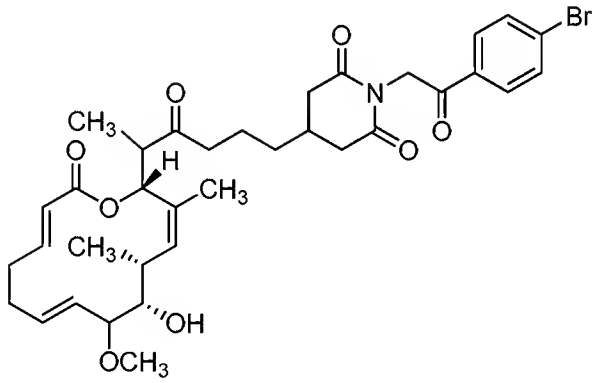
REMARKS

The claims pending in the Application after entry of the present Amendment will be claims 1-62. Claim 1 has been amended to add a compound to the proviso as discussed below in Section II. Additionally, claims 1, 11-15, 23-25 and 32-40 have been amended to revise the scope of the genus presented by Applicant, as discussed in detail below in Section III; wherein exemplary support for such amendments are detailed in Table II. Further, claims 13, 15, 23, 32 and 33 have been amended to change "alkylidene" to "alkylenyl" and to change "alkenylidene" or "alkenylenyl" in order to conform to more standard chemical nomenclature practice. Exemplary support for this amendment is found in paragraph [0321], the second compound in the third row. No new matter has been added by these amendments.

I. Rejection under 35 U.S.C. §102(b)

Claim 1 is rejected under 35 U.S.C. §102(b) as being anticipated by Nakamura et al. (Journal of Antibiotics (2002), 55(4), 442-444). According to the Examiner, Nakamura et al. anticipates claim 1 because it teaches N-p-bromophenacylmigrastatin:



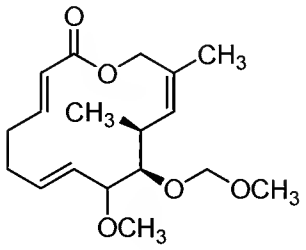
As an initial matter, Applicant notes that the present claims are directed to **compositions** which include a therapeutically effective amount of, together with a pharmaceutically acceptable carrier, adjuvant, or vehicle. Nakamura et al. teaches isolated compounds and provides no teaching or suggestion of a *composition* as recited in the present claims.

Moreover, the compounds of Formula I recited in the present claims do not include N-p-bromophenacylmigrastatin, the compound described by Nakamura et al.

For at least these reasons, Applicant respectfully submits that Nakamura et al. cannot anticipate (or render obvious) the presently claimed invention; the rejection should be removed.

II. **Rejection under 35 U.S.C. §102(b)**

Claims 1-12, 14, 16-19, 27 and 30 are rejected under 35 U.S.C. §102(b) as being anticipated by Gaul et al. (Tet. Lett. (2002), 43(50), 9039-9042). According to the Examiner, Gaul et al. anticipates these claims because it teaches synthesis of the macrolide core **13** of migrastatin:



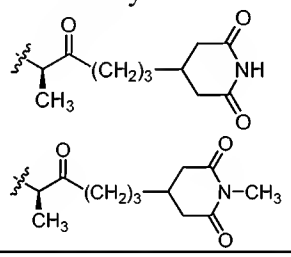
As an initial matter, Applicant notes that the present claims are directed to **compositions** which include a therapeutically effective amount of, together with a pharmaceutically acceptable carrier, adjuvant, or vehicle. Gaul et al. teaches isolated compounds and provides no teaching or suggestion of a *composition* as recited in the present claims. However, in order to expedite prosecution of the instant case, Applicant has added the cited compound (i.e., macrolide core **13**) to the proviso in claim 1. Applicant asserts that the rejection is now moot. As such, Applicant respectfully requests that this rejection be withdrawn.

III. **Rejection under 35 U.S.C. §112, para. 1**

Claims 1-40, 43-57, and 60-62 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. However, the Examiner acknowledged that the specification specifically discloses (and therefore describes) at least 23 different compounds within the scope of Formula I, which compounds support, according to the Examiner, the following definitions:

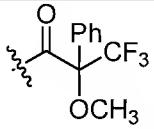
Table 1

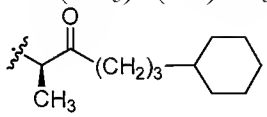
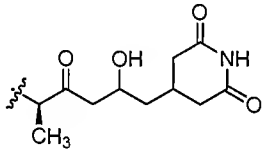
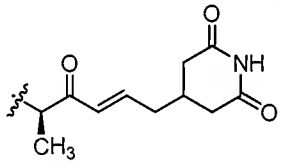
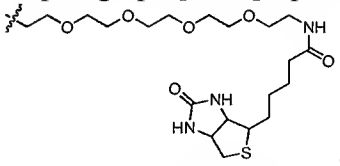
Variable	Defintion
R_1, R_2, R_5, R_6	H lower alkyl
R_3	H lower alkyl
R_4	H OH

	-O(lower alkyl), i.e., "lower alkoxy"
R_a, R_b, R_c	H
Y_1 and Y_2	H Me, i.e., "lower alkyl" combined to (=O), =N (as provided in Table of compounds at page 7 of the Office action), OH CF_3 -O(lower alkyl)
n	3
X_1	O NH CH_2
Q	H lower alkyl 

Applicant appreciates the Examiner's acknowledgement that these definitions are supported by the present specification, and specifically by the compounds actually reduced to practice in the specification. Applicant respectfully submits, however, that there is no justification for limiting the present claims to specifically those embodiments that have been reduced to practice in the specification. At a minimum, the present specification supports claims to specifically depicted species, whether or not they were actually reduced to practice. Applicant further points out that the Examiner's list of supported definitions does not even include all of the species present in compounds that the Examiner lists on page 7 of the Office Action. Applicant respectfully submits that the present specification fully supports at least the following additional species for listed variables:

Table 2

Variable	Additional Species
R_1, R_2, R_5, R_6	-
R_3	-
R_4	 , specification page 16

	-NH_2, specification page 25 halo, (fluoro compound at) specification page 25 H, compound 45, specification page 157 -$OC(=O)CH_3$, compound 49, specification page 158 Support for R_4 "protecting groups" -O-benzyl, specification page 11 -OMOM, compound 15, specification page 147 -OTBS, compound 47, specification page 158 oxo, compound 50, specification page 158
R_a, R_b, R_c	-
Y_1 and Y_2	-
n	-
X_1	-
Q	-$CH(CH_3)C(=O)CH_3$, paragraph [0321], specification page 137  , paragraph [0321], specification page 137  , paragraph [0321], specification page 137  , paragraph [0321], specification page 137
R^{Y1} and R^{Y2}	heteroaliphatic, compound 73, specification page 163 H, paragraph [0321], specification page 137  , i.e., "aliphatic" and "heteroaliphatic", compound 73, specification page 163
W	O and NH, compound 73, specification page 163
R_7	lower alkyl, all compounds except the last two, specification page 137 heteroalkyl, compound 73, specification page 163
R_8	alkyl, compound 73, specification page 163, and paragraph [0321], specification page 137 heteroalkyl, paragraph [0321], specification page 137 cycloalkyl, paragraph [0321], specification page 137 heterocycloalkyl, compound 73, specification page 163, and paragraph [0321], specification page 137
X, Y and Z	bond, all compounds except the last two, specification page 137 -O-, compound 73, specification page 163

	-C(O)-, compound 73, specification page 163 -NH, compound 73, specification page 163
$\mathbf{R^Y}$	H, paragraph [0321], specification page 137 $-OR^{Y1}$, to form –OH, paragraph [0321], specification page 137
r	integer from 1 to 6, paragraph [0321] compounds, specification page 137
$\mathbf{R^{8A}/R^{8B}}$	H and lower alkyl, paragraph [0321] compounds, specification page 137

The present Amendment amends the claims to recite those species presented in Tables 1 and 2. The present specification fully describes the amended claims. Therefore, Applicant respectfully requests withdrawal of the rejection under 35 U.S.C. §112, para. 1, for lack of written description.

IV. Rejection under 35 U.S.C. §112, para. 1

The Office Action includes a rejection of claims 48-62 are rejected under 35 U.S.C. §112, first paragraph, on the ground that "the specification does not reasonable provide enablement for treating breast tumor metastasis in a subject. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims" (page 9 of the Office Action).

On November 4, 2008, Applicant telephoned the Examiner to clarify whether the levied rejection represented a challenge to the quality of Applicant biological data included in the present application (as not being predictive of therapeutic effect in the treatment of breast cancer metastais) or whether it was intended as an objection to the scope of Applicant's genus. The Examiner indicated that he was not challenging the biological data but rather the scope of the genus presented. The Examiner further indicated that he would be amenable to removing the lack of enablement rejection if Applicant presented a more contained genus of compounds, and further that he would be willing to consider a broader genus than the particular compound scope proposed in the Office Action at pages 7-8, provided that Applicant presented an explanation justifying additional changes to that proposed genus. Such an explanation is provided above.

Applicant therefore submits that the present amendment, which narrows the claimed genus of compounds present within a recited composition, obviates the rejection for lack of enablement. The rejection can therefore be removed.

V. **Rejection under 35 U.S.C. §112, para. 2**

Claims 43-44 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Specifically, the Examiner asserts that it is not clear what amount is meant by the term "an amount effective to inhibit metastasis/angiogenesis" (see office action, page 10).

Applicant respectfully traverses this rejection. One skilled in the art would understand from the specification and claims that the phrase "an amount effective to inhibit metastatis/angiogenesis" is a phrase utilized to illustrate a means of "administering to a subject in need a therapeutically effective amount of the compound of the invention" (see page 129, paragraph [0295]). In particular, the specification at page 132, paragraph [0306] further defines the expression "effective amount" to refer to "a sufficient amount of agent to inhibit the growth of tumor cells, or refers to a sufficient amount to reduce the effects of cancer. The exact amount required will vary from subject to subject, depending on the species, age, and general condition of the subject, the severity of the diseases, the particular anticancer agent, its mode of administration, and the like." (see paragraph [-0306], specification pages 132-133). Moreover, not only does the specification provide particular guidance with respect to "dosage unit forms" at paragraph [0307], but paragraph [0308] then provides specific dosage level embodiments. Therefore, given the specification guidance discussed above, it is clear that one skilled in the art would understand what the phrase "an amount effective to inhibit metastatis/angiogenesis" means, and moreover, the specification allows one to point to specific dosages provided in the specification.

Applicant submits that each of claims 43 and 44 meet the requirements of 35 U.S.C. §112, second paragraph, and respectfully requests withdrawal of this rejection.

Applicants invite the Examiner to contact the undersigned, Julie Anne Knight, at (617) 248-5227 with any questions pertaining to the above-identified application in order to expedite prosecution of this case.

Respectfully submitted,

Dated: December 5, 2008

/Julie Anne Knight/
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